CLINICAL CASES
Case: Ms. MC
Patient Profile

• 35-year-old female, accountant
• Non-smoker, does not drink alcoholic beverages
• Presents at the ER complaining of difficulty urinating
• Started to experience difficulty urinating about a year ago
  – Also increased frequency and pain
  – Febrile episodes; Tmax = 38.6°C
Ms. MC's History: 1 Year Ago

- Urinalysis: pyuria = 20-30 pus cells/hpf
- **Diagnosis:** urinary tract infection
- **Treatment:** 500 mg ciprofloxacin q 12 h x 7 days
  - Repeat urinalysis showed no infection

hpf = high power field
Discussion Questions

Based on the case presentation, what would you consider in your differential diagnosis?

What further history would you like to know?

What tests or examinations would you conduct?
Signs and Symptoms of Interstitial Cystitis

- Chronic pelvic pain
- Pain between vagina and anus (women) or scrotum and anus (men)
- Persistent, urgent need to urinate
- Frequent urination – often small amounts – throughout the day and night
  - Up to 60 times/day
- Pain/discomfort while bladder fills
- Relief after urination
- Painful sexual intercourse

Burden of Interstitial Cystitis

- Frequent urination
- Bladder pain
- Decreased physical functioning
- Decreased ability to function in normal role
- Decreased vitality
- Decreased social functioning
- Decreased sexual functioning

Quality of life of patients with interstitial cystitis is poorer than that of patients undergoing dialysis for ESRD

ESRD = end-stage renal disease
Causes of Interstitial Cystitis (IC)

- Exact causes unknown
  - Likely involves many factors
  - May include autoimmune reaction, genetics, infection, or allergy
- Patients with IC may also have a defect in bladder epithelium
- May be a bladder manifestation of a more general inflammatory condition

Some IC symptoms resemble those of bacterial infection but urine cultures indicate no infection

Ms. MC: Past Medical History

- Migraines since the age of 20
- Unremarkable gynecologic history
- Occasional dysmenorrhea
- Family history (mother) of hypertension
Ms. MC: 10 Months Ago...

- Experienced subrapubic pain
  - Intermittent and crampy
  - Increased frequency of urination
    - Nocturia: sometimes 3-4 times nightly
- Dyspareunia
- Symptoms resolved spontaneously after a few days so she did not consult her physician
Ms. MC: 7 Months Ago...

- Recurrence of suprapubic pain
- Radiating to lower abdomen
- Increased urinary frequency and nocturia
- Consulted physician
  - Urinalysis = normal
  - Treatment = analgesics (paracetamol, mefenamic acid)
    - Did not provide symptom relief
Ms. MC: Gynecological Consult

- 3 months ago
- Results unremarkable
  - Normal speculum and pelvic exams
  - Normal Pap smear
Ms. MC: Urology Consult

- 3 months ago
- Cystoscopy
  - Multiple submucosal hemorrhages over posterior wall of urinary bladder
  - Glomerulations
- Cystometry
  - Increase in pain during bladder filling; relieved with bladder emptying
- Bladder biopsy: no carcinomatous lesions
Ms. MC: History

- Patient continues to experience relentless pain over suprapubic area
  - Pain medications do not work
- Sleepless nights due to nocturia
- Reduced sex drive
- Depressed
Discussion Question

WHAT WOULD BE YOUR DIAGNOSIS FOR THIS PATIENT?
Diagnosis

- This patient has interstitial cystitis.
Discussion Question

WHAT TREATMENT STRATEGY WOULD YOU RECOMMEND?
# Treatment of Interstitial Cystitis

| Non-pharmacological          | • Avoidance of trigger foods  
|                              | • Dietary supplementation  
|                              | • Stress relieving exercises  
|                              | • Transcutaneous nerve stimulations (TENS)  
| Oral medication              | • Antihistamines  
|                              | • Antidepressants  
|                              | • Cimetidine  
|                              | • Sodium pentosanpolysulfate  
|                              | • L-arginine  
|                              | • Prelief  
|                              | • Oxybutinin  
|                              | • Antibiotics  
|                              | • Methenamine  
| Drugs for bladder instillation | • Hylauronic acid  
|                              | • Chondroitin sulfate  
|                              | • Dimethylsulfoxide (DMSO)  
|                              | • Intravesical heparin  
|                              | • Hydrodistension  
| Surgery                      | • Partial cystectomy  
|                              | • Augmentation cystoplasty  
|                              | • Urinary diversion  

WOULD YOU MAKE ANY CHANGES TO THERAPY OR CONDUCT FURTHER INVESTIGATIONS?
Ms. MC: Follow Up

- A full gynecologic and urologic examination and diagnostic tests were done
Case: Mr. AD
Mr. AD: History

- 38-year-old male journalist
- 8-year history of bowel problems
- Complains of intermittent abdominal cramping, bloating, and urgent loose stools
  - “Bad days” occur 2 or 3 times per week
- Describes lower abdominal cramping that is relieved after 1 or 2 loose stools
- Reports his symptoms are worse after eating
  - Significant impact on his personal and work life
- Avoids going to restaurants
  - Usually skips meals on work days to prevent an urgent need to use the bathroom while driving
Mr. AD: History

- Previous treatments: antispasmodics, a probiotic, and an antibiotic.
- Antidiarrheal agents sometimes provided transient relief but led to constipation
- Short course of amitriptyline: sedative side effects; medication was intolerable
- Denies rectal bleeding, fevers, or weight loss
- Thinks his mood affects his symptoms
  - Believes stress may be an exacerbating factor
- No family history of gastrointestinal diseases or cancer
- Has been trying to avoid fatty and greasy foods
  - Not sure if it has been helpful
- Wondering if there are any other options – including nonmedical strategies – to address his symptoms
Which of the following would you use to make the diagnosis in Mr. AD? Why?

- Colonoscopy with biopsies
- Breath test for small intestinal bacterial overgrowth
- ROME III criteria
- Thyroid-stimulating hormone and celiac serologies
Mr. AD: Clinical Examination and Pain Assessment

- Good health
  - Mild obesity (body mass index = 29 kg/m$^2$)
- Clinical examination
  - Abdomen is soft, mildly tender diffusely with some mild distention
  - No organomegaly
- Previous laboratory results show no anemia
- Celiac serologies negative
- Colonoscopy (1 year ago): normal colonic and terminal ileal mucosa with normal random biopsies
WHAT WOULD BE YOUR DIAGNOSIS FOR THIS PATIENT?
Rome III Diagnostic Criteria for Irritable Bowel Syndrome (IBS)

- Symptom onset ≥6 months prior to diagnosis
- Recurrent abdominal pain or discomfort ≥3 days per month in the last 3 months associated with ≥2 of the following:
  - Improvement with defecation
  - Onset associated with a change in stool frequency
  - Onset association with a change in stool form (appearance)
- ≥1 of the following symptoms on at least one quarter of occasions for subgroup identification:
  - Abnormal stool frequency (<3/week)
  - Abnormal stool form (lumpy/hard)
  - Abnormal stool passage (straining, incomplete evacuation)
  - Bloating or feeling of abdominal distension
  - Passage of mucous
  - Frequent, loose stools

Rome III Diagnostic Criteria for Irritable Bowel Syndrome (IBS)

• Three subgroups of IBS:
  • IBS with diarrhea (IBS-D) (more common in men)
  • IBS with constipation (IBS-C) (more common in women)
  • IBS with mixed bowel habits

• Each group accounts for about one third of all patients.
Mr. AD: What Is the Diagnosis?

- Patient fulfills Rome III criteria for **IBS**:  
  - >6 months of recurrent abdominal pain/discomfort ≥3 days per month within the last 3 months  
  - Pain/discomfort improves with defecation  
  - Onset of symptoms associated with a change in frequency or form of stool  
- Patient fulfills criteria for **IBS with diarrhea** (IBS-D):  
  - Loose (mushy) or watery stools ≥25% of the time and hard or lumpy stools <25% of bowel movements  
  - Also some classic IBS symptoms (bloating, urgency, heightened gastrocolic reflex)
Mr. AD: What Is the Diagnosis?

Mr. AD was diagnosed with irritable bowel syndrome with diarrhea (IBS-D)
Irritable Bowel Syndrome (IBS)

• ≤20% of adults experience symptoms compatible with IBS
• Defined by recurring abdominal pain with altered bowel habits
  • No structural or easily identifiable biochemical abnormality
• Possible factors in IBS pathogenesis:
  • Disturbances in motility
  • Brain-gut axis
  • Genetic factors
  • Impaired gut barrier function
  • Mucosal immunologic function
  • Gut microbiome
  • Psychosocial factors

Differential Diagnosis of Irritable Bowel Syndrome (IBS)

IBS = irritable bowel syndrome
Brain-Gut Axis in Visceral Pain

Cognitive, emotional, and autonomic centres in the brain

Brain-gut axis

Neuroendocrine centres, enteric nervous system, and immune system

Altered brain-gut interactions can contribute to autonomic dysregulation of the gut and associated pain and perceptual changes in visceral disorders

Discussion Question

What would you tell this Mr. AD is the cause of his IBS symptoms?

• Underlying anxiety and depression
• History of sexual abuse
• Malabsorption
• Genetic predisposition in the face of an insult

IBS = irritable bowel syndrome
Putative Model of IBS Development

IBS = irritable bowel syndrome
Discussion Question

WHAT TREATMENT STRATEGY WOULD YOU RECOMMEND?
What is the best treatment for IBS?
Multimodal Approach to IBS Treatment

The multiple symptoms of IBS require a multidisciplinary approach to treatment, including medications, diet and nonpharmacological methods.

IBS = irritable bowel syndrome
The prescription of which of the following agents for Mr. AD would be based on high-quality randomized trials demonstrating efficacy?

- Loperamide
- Diphenoxylate
- Alosetron
- Octreotide
Evidence-Based Treatments for IBS-D

<table>
<thead>
<tr>
<th>Drug</th>
<th>Global Symptoms</th>
<th>Pain</th>
<th>Bloating</th>
<th>Stool Frequency</th>
<th>Stool Consistency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alosteron</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Antibiotics (rifaximim)</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidepressants</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Loperamide</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Antispasmodics</td>
<td>+/-</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probiotics (bifidobacteria, some combinations)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

IBS-D = irritable bowel syndrome with diarrhea
### Medications for Diarrhea in IBS-D

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side Effects</th>
<th>Evidence</th>
<th>FDA Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>For Symptom</td>
<td>For IBS</td>
</tr>
<tr>
<td>Loperamide</td>
<td>Constipation</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td></td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Desipramine</td>
<td></td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>SSRIs</td>
<td>Sexual dysfunction, headache, nausea, sedation, insomnia, sweating, withdrawal symptoms</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Paroxetine</td>
<td></td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Citalopram</td>
<td></td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td></td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

IBS-D = irritable bowel syndrome with diarrhea; SSRI = selective serotonin reuptake inhibitor
## Medications for Constipation in IBS-C

<table>
<thead>
<tr>
<th>Drug</th>
<th>Side Effects</th>
<th>Evidence</th>
<th>FDA Approved</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>For Symptom</td>
<td>For IBS</td>
<td>For Symptom</td>
</tr>
<tr>
<td>Laxatives and Secretory Stimulators</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polyethylene glycol 3350</td>
<td>Diarrhea, bloating, cramping</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Lactulose</td>
<td>Diarrhea, bloating, cramping</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Lubiprostone</td>
<td>Nausea, diarrhea, headache, abdominal pain and discomfort</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Prokinetics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tegaserod</td>
<td>Initial diarrhea, abdominal pain, cardiovascular ischemia (rare)</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>

**IBS-C** = irritable bowel syndrome with constipation

Abdominal Pain in IBS

- Antispasmodics (hyoscyamine, mebeverine) have been used to treat pain
  - No data from high quality RCTs of effectiveness in reducing pain or global symptoms
- Tricyclic antidepressants commonly used
  - Often in low doses (e.g., 10-75 mg amitriptyline)
- Several small, randomized, controlled trials suggest SSRIs may have beneficial effects in patients with IBS
  - Especially effective in improving general well-being
  - Some studies indicate positive effects on abdominal pain
- High prevalence of coexisting anxiety in patients with IBS
  - Benzodiazepines are not recommended for long-term therapy
    - Risk of habituation and potential for dependency

IBS = irritable bowel syndrome; RCT = randomized controlled trial; SSRI = selective serotonin reuptake inhibitor
Discussion Question

Which of the following would you limit if you were to recommend a FODMAP-restricted diet for this patient?

- Fructose, lactose, cellulose
- Fructose, fructans, pectins
- Fructose, cellulose, pectins
- Sorbitol, fructans, raffinose

FODMAP = Fermentable Oligo-Di-Monosaccharides and Polyols
Low FODMAPs: A Dietary Approach to IBS

• FODMAPs = poorly absorbed, short-chain carbohydrates
• Highly fermentable by gut bacteria
• Fermentation $\rightarrow$ gas and increased fluid load
  - Secondary luminal distension + peristalsis in distal small bowel and proximal colon $\rightarrow$ diarrhea, bloating, cramping

Evidence suggests a FODMAP-reduced diet may provide a 20% therapeutic advantage over a standard diet

FODMAP = Fermentable Oligo-Di-Monosaccharides and Polyols; IBS = irritable bowel syndrome
## FODMAP Dietary Recommendations

<table>
<thead>
<tr>
<th>FODMAP</th>
<th>Fructose</th>
<th>Polyols</th>
<th>Lactose</th>
<th>Fructans, Galactans</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High FODMAP</strong></td>
<td>Apples, pears, watermelon, honey, fruit juices, dried fruits,</td>
<td>Sugar, alcohols,* stone fruits, avocado, mushrooms, cauliflower</td>
<td>Milk,† yogurt, soft cheeses (ricotta, cottage)</td>
<td>Wheat, rye, garlic, onions, artichokes, asparagus, inulin, soy, leeks, legumes,</td>
</tr>
<tr>
<td></td>
<td>high-fructose corn syrup</td>
<td></td>
<td></td>
<td>lentils, cabbage, Brussels sprouts, broccoli</td>
</tr>
<tr>
<td><strong>Alternative</strong></td>
<td>Citrus, berries, bananas, grapes, honeydew, cantaloupe, kiwifruit</td>
<td>Sweeteners, including sugar, glucose, other artificial sweeteners not</td>
<td>Lactose-free dairy products, rice milk, hard cheeses</td>
<td>Starches (rice, corn, potato, and quinoa), vegetables</td>
</tr>
<tr>
<td><strong>Lower FODMAP</strong></td>
<td></td>
<td>ending in &quot;ol&quot; (sucralose, aspartame are good)</td>
<td></td>
<td>(winter squash, lettuce, spinach, cucumbers, bell peppers, green beans, tomato,</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>eggplant)</td>
</tr>
</tbody>
</table>

*Sorbitol, maltitol, mannitol, xylitol, isomalt  †Cow, goat, sheep  
FODMAP = Fermentable Oligo-Di-Monosaccharides and Polyols  
Cognitive Behavioral Therapy (CBT) for IBS

• Best studied psychological treatment for IBS
• Cognitive techniques (group or individual, 4 to 15 sessions) aim to change catastrophic or maladaptive thinking patterns underlying the perception of somatic symptoms
• Behavioral techniques aim to modify dysfunctional behaviors through relaxation techniques, contingency management (rewarding healthy behaviors), or assertion training
• Some RCTs have also shown reductions in IBS symptoms with the use of gut-directed hypnosis

IBS = irritable bowel syndrome; RCT = randomized controlled trial
Mr. AD: Therapeutic Approach

- A lot of Mr. AD’s first visit was spent reviewing the etiology, pathophysiology, and treatment of IBS with him
- A low-FODMAP diet administered under the guidance of a registered dietician who is familiar with this diet was recommended
- He was referred for cognitive behavioral therapy
- He was also seen by a psychiatrist for hypnotherapy
WOULD YOU MAKE ANY CHANGES TO THERAPY OR CONDUCT FURTHER INVESTIGATIONS?
Mr. AD: Follow-up

6 weeks
- Mr. AD states that he feels 40%-45% better

3 months
- Mr. AD notes a 70%-75% improvement in his symptoms
Mr. AD: Case Conclusion

- Mr. AD’s presentation represents moderately severe IBS-D because his symptoms are longstanding and lifestyle altering, but they are not incapacitating.
- He has tried multiple medications in the past, including antispasmodics and antidiarrheal medications, but ultimately did not find them helpful.
- Often in these types of cases a low-dose TCA would be recommended, but he has been intolerant to these medications in the past.
- He has also tried a probiotic and possibly rifaximin for his IBS-D without much success.
- Given his lack of response and intolerance to multiple medications, he was motivated to follow through with diet modification and cognitive behavioral therapy for his IBS symptoms.

IBS-D = irritable bowel syndrome with diarrhea; TCA = tricyclic antidepressant
While it is natural for providers to initially presume that the complexity of the low-FODMAP diet guarantees patient non-adherence, patients with IBS often desire a more holistic approach to their care. They often are interested in learning about dietary interventions, especially when symptom onset is related to eating a meal. Such patients are often already on highly restrictive diets; they are therefore highly motivated to follow structured, evidence-based dietary interventions.

The treatment of IBS-D requires a multifaceted approach that includes finding the optimal combination of the pharmacotherapeutic, dietary, and behavioral treatments.

FODMAP = Fermentable Oligo-Di-Monosaccharides and Polyols; IBS-D = irritable bowel syndrome with diarrhea
Red Flags for Differential Diagnosis in 
IBS

• Symptom onset after age 50 years
• No rectal bleeding
• No significant changes in blood tests (e.g., unexplained iron deficiency anemia)
• No fever
• No unexplained weight loss
• No abdominal mass
• No family history of cancer, gastrointestinal disease
• No evidence of inflammatory, anatomic, metabolic, or neoplastic process

IBS = irritable bowel syndrome
Case: Mrs. RL
Mrs. RL: Profile

- 33-year-old female housewife
- Complains of vulvar discomfort described as burning
  - Has been occurring for the last 9 months
Mrs. RL: Physical Exam

- No sign of vaginal infection (*e.g.*, herpes, candidiasis), inflammation (*e.g.*, lichen sclerosis), or neoplasia
- Cotton swab touching 6 vestibular sites was described as painful
- Brush allodynia positive for most painful vestibule area
- DN4 questionnaire score = 5/10
DN4

- Completed by physician in office
- Differentiates neuropathic from nociceptive pain
- 2 pain questions (7 items)
- 2 skin sensitivity tests (3 items)
- Score ≥4 is an indicator for neuropathic pain
- Validated

DN4 = Douleur neuropathique en 4 questions
Mrs. RL: History

• Mrs. RL admits she suffers from anxiety
• She is also having marital difficulties

Medical history

• Interstitial cystitis (painful bladder, frequency, urgency, nocturia with no known cause)
• Fibromyalgia
Discussion Questions

Based on the case presentation, what would you consider in your differential diagnosis?

What further history would you like to know?

What tests or examinations would you conduct?
Mrs. RL: Further Tests/Examinations

- **Dermatological examination**: no evidence of edema, erythema, pallor, or hyperpigmentation
- **Neurological examination**: No evidence of hypoesthesia in pudental nerve distribution, but brush allodynia (+) and pinprick hyperalgesia (+) in the vulvar region, posterior introitus
- **Gynecological examination**: No evidence of tumor, infection
Further Tests/Examinations - Results

- Vaginal smear test: negative for neoplastic changes
- Vaginal wet mount, KOH stain, fungal culture and Gram stain: negative for Candidiasis/yeast or bacterial infection
Differential Diagnosis of Vulvar Pain and Dyspareunia

Discomfort with intercourse or at the vulvar region for at least three months?

Yes

Does the patient have dermatologic changes other than erythema or edema, pain not localized to the vulva, or Candida identified by KOH microscopy or culture?

No

Does examination of external vulva indicate sensitivity to mild pressure from a cotton swab (3- to 5-mm indentation), especially at the posterior introitus or hymenal remnants?

Yes

Diagnosis of vulvodynia likely

No

Consider differential diagnosis (Table 2).

Evaluate with normal saline and KOH microscopy, culture, or biopsy, or other testing as indicated.

No diagnosis

Go to A

Positive findings

Treat for other diagnoses.

Continued vulvar sensitivity?

Yes

Reevaluate.
ISSVD Vulvodynia Pattern Questionnaire

What are your symptoms? (circle all that apply)
- burning
- stinging
- rawness
- irritation
- soreness
- itching
- stabbing
- knife-like
- paper-cuts
- aching
- other

Which of the following problems do you have? (circle)
- Fibromyalgia
- High blood pressure
- Frequent headaches
- Angina pectoris/heart attacks
- Frequent urinary tract infections
- Diabetes mellitus
- Chronic fatigue syndrome
- Genital herpes
- Low energy levels
- Thyroid disease
- Depression
- Sinus problems/hay fever
- Difficulty sleeping
- Allergies to medications
- Weight gain or loss of more than ten pounds unintentionally in the past six months
- TMJ syndrome (temporomandibular joint)
- Back pain
- Pelvic pain

Which of the following produces pain?
- Sexual intercourse
  - If yes,
    - With penetration
    - During intercourse
    - After intercourse
    - With all partners
- Insertion of tampon
- Tight clothing or blue jeans

Full questionnaire

ISVVD = International Society for the Study of Vulvovaginal Disease
Vulval Pain Functional Questionnaire

1. Because of my pelvic pain
   - 3 I can’t wear tight-fitting clothing like pantyhose that puts any pressure over my painful area.
   - 2 I can wear closer fitting clothing as long as it only puts a little bit of pressure over my painful area.
   - 1 I can wear whatever I like most of the time, but every now and then I feel pelvic pain caused by pressure from my clothing.
   - 0 I can wear whatever I like; I never have pelvic pain because of clothing.

2. My pelvic pain
   - 3 Gets worse when I sit, so it hurts too much to sit any longer than 30 minutes at a time.
   - 2 Gets worse when I sit. I can sit for longer than 30 minutes at a time, but it is so painful that it is difficult to do my job or sit long enough to watch a movie.
   - 1 Occasionally gets worse when I sit, but most of the time sitting is comfortable.
   - 0 My pain does not get worse with sitting, I can sit as long as I want to.
   - 0 I have trouble sitting for very long because of another medical problem, but pelvic pain doesn’t make it hard to sit.

6. Because of my pelvic pain
   - 3 I don’t get together with my friends or go out to parties or events.
   - 2 I only get together with my friends or go out to parties or events every now and then.
   - 1 I usually will go out with friends or to events if I want to, but every now and then I don’t because of the pain.
   - 0 I get together with friends or go to events whenever I want, pelvic pain does not get in the way.

10. Because of my pelvic pain
    - 3 It hurts too much for my partner to touch me sexually even if the touching doesn’t go in my vagina.
    - 2 My partner can touch me sexually outside the vagina if we are very careful
    - 1 It doesn’t usually hurt for my partner to touch me sexually outside the vagina, but every now and then it does hurt
    - 0 It never hurts for my partner to touch me sexually outside the vagina
    - 0 This question does not apply to me because I don’t have a sexual partner.
    - 0 Specifically, I won’t get involved with a partner because I worry about pelvic pain during sex.

Vulval Pain Questionnaire

Indicate the effect which the following have on your discomfort:

[On the list, circle the best treatments and underline the worst treatments]

<table>
<thead>
<tr>
<th>Effect</th>
<th>Relief</th>
<th>No change</th>
<th>Worsens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heat (like a hot bath)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cold (like a cool compress)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sexual activity - (does not have to be intercourse)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underwear</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Friction (rubbing or scratching)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

My discomfort usually causes

- NO interference with daily routine or planned activities
- SOME interference with daily routine or planned activities
- An interruption in daily routine or planned activities
- Confinement to bed
- The pursuit of immediate medical attention

Please mark the squares which best show the location of your symptoms

- Mons pubis area
- Clitoris
- Labia majora
- Labia minora
- Urethra (bladder opening)
- Vestibule (inside vulva)
- Vagina (within the vestibule)
- Anal area

Diagram showing the location of symptoms:

- Mons Pubis
- Clitoris
- Labia majora
- Labia minora
- Urethra
- Vestibule (entrance to the vagina)
- Perineum
- Anus

WHAT WOULD BE YOUR DIAGNOSIS FOR THIS PATIENT?
Signs and Symptoms of Vulvodynia

- Pain in genital area:
  - Burning
  - Soreness
  - Stinging
  - Rawness
  - Painful intercourse
  - Throbbing
  - Itching

- Occasional or constant pain that can last for month or years

Causes of Vulvodynia

• Exact causes unknown
• Possible contributors:
  – Injury to or irritation of nerves of vulvar region
  – Past vaginal infections
  – Allergies or sensitive skin
  – Hormonal changes
• Some women with vulvodynia have a history of sexual abuse

Most women with vulvodynia have no known causes
Burden of Vulvodynia

- Chronic vulvar discomfort
- Common descriptors:
  - Itching
  - Burning
  - Periodic knife-like or sharp pain
  - Excessive pain on contact to the genital area
- Compromises ability of sufferers to enjoy life
- Quality of life is lower than in kidney transplant recipients

Many women with vulvodynia feel out of control of their lives, and vulvodynia has a severe negative impact on their sex lives.
# Vulvodynia: Factors Affecting Pain

<table>
<thead>
<tr>
<th>Factors that Exacerbate Pain</th>
<th>Factors that Relieve Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Intercourse</td>
<td>• Loose clothing</td>
</tr>
<tr>
<td>• Tight clothes</td>
<td>• Not wearing underwear</td>
</tr>
<tr>
<td>• Partner touch</td>
<td>• Applying ice to the area</td>
</tr>
<tr>
<td>• Riding a bicycle</td>
<td>• Being distracted</td>
</tr>
<tr>
<td>• Use of tampons</td>
<td>• Lying down</td>
</tr>
<tr>
<td>• Prolonged sitting</td>
<td></td>
</tr>
</tbody>
</table>

Comorbidities of Vulvodynia

- Psychological distress
- Fibromyalgia
- Irritable bowel syndrome
- Repeated yeast infections
- Chronic fatigue syndrome
- Dyspareunia
- Interstitial cystitis

Discussion Question

WHAT TREATMENT STRATEGY WOULD YOU RECOMMEND?
Proposed Treatment Algorithm for Vulvodynia

Positive Clinical Diagnosis based on:
Medical History
Physical examination and specific tests
Electromyography and vaginal pressure of the pelvic floor muscles
Biopsy and histological examinations

FIRST Therapeutic Step

YULAR CARE MEASURES
- Prevent detergent or softeners left on underwear,
- Use lubricants for intercourse
- Use mild soaps for hygiene
- Avoid wearing tight pants or panty area genital

DIETARY RECOMMENDATIONS
- Low-oxalate food intake
- Calcium citrate Supplementation

TOPICAL MEDICATIONS
- Lidocaine gel (2%–5%)
- Estradiol vaginal cream
- Amitriptyline 2% + Baclofen 2% cream
- Gabapentin 200–400 mg in a liposomal base
- 0.025% Capsaicin cream
- Nitroglycerin 0.2% cream
- Cauterous lysate cream human cytokines

ORAL MEDICATIONS
- Tricyclic antidepressants
- SNRI mood stabilizers
- Neuromodulators
- Anticonvulsants

BIOFEEDBACK / PHYSICAL THERAPY

COGNITIVE BEHAVIORAL THERAPY
SEXUAL COUNSELLING

2–3 Months Treatment → Good Relief → Stop Treatment When Indicated

Inadequate / Insufficient Relief

SECOND Therapeutic Step

MULTILEVEL INFILTRATION
- Trigger point injection and local anesthetic injections
- Intraepidermal sympathetic block
- Botulinum Toxin

Radiofrequency (RF) procedures
- Incisional Ganglion ablation
- RF sacral rhizotomy
- Percutaneous sacral nerve root modulation with pulsed RF

Neurostimulation procedures
- Intravaginal transcutaneous electrical nerve stimulation
- Spinal cord stimulation
- Selective stimulation of sacral nerve roots S2/S3/L4
- Subcutaneous vulvar stimulation

Maintenance of first step
YULAR CARE MEASURES
BIOFEEDBACK / PHYSICAL THERAPY
COGNITIVE BEHAVIORAL / SEXUAL COUNSELLING

2–3 Months Treatment → Good Relief → Stop Treatment When Indicated

Inadequate / Insufficient Relief

THIRD Therapeutic Step

SURGERY
- Local Excision
- Vestibuloplasty
- Perineoplasty
- Surgery on pudendal nerve entrapment
Treatment Options for Vulvodynia

- Oral pharmacological therapies
  - Amitriptyline, calcium citrate, desipramine, gabapentin, paroxetine, venlafaxine
- Topical therapies
  - Lidocaine, avoidance of irritants
- Dietary changes
  - Low oxalate diet
- Surgical therapy
  - Perineoplasty, vestibulectomy
- Other therapies
  - Biofeedback, physical therapy, cognitive behavioral therapy
## Oral Therapies for Vulvodynia

<table>
<thead>
<tr>
<th>Drug</th>
<th>Proposed Mechanism</th>
<th>Side Effects</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>Decreases neuronal hypersensitivity</td>
<td>Dry mouth, fatigue (often transient), constipation, weight gain (uncommon)</td>
<td>Case reports</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Retrospective reports</td>
</tr>
<tr>
<td>Calcium citrate</td>
<td>Decreases oxalate deposition in tissues</td>
<td>Minimal</td>
<td>Case reports</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Anecdotal reports</td>
</tr>
<tr>
<td>Desipramine</td>
<td>Decreases neuronal hypersensitivity</td>
<td>Same as amitriptyline but less common</td>
<td>None. Based on similarity to amitriptyline.</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>Decreases neuronal hypersensitivity</td>
<td>Headaches, nausea, vomiting, fatigue, dizziness (often transient or mild)</td>
<td>Case reports</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Decreases neuronal hypersensitivity</td>
<td>Rarely fatigue, anorgasmia, or weight gain</td>
<td>Case report</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>Decreases neuronal hypersensitivity</td>
<td>Anorgasmia, GI side effects, anxiety</td>
<td>Used in other painful neuropathies</td>
</tr>
</tbody>
</table>

GI = gastrointestinal
Mrs. RL: Treatment

- **Oral medication**: amytriptyline titrated up to 50 mg/night

- **Topical treatment**: Emla cream, max: 12 hours/day

- **Cognitive behavioral therapy**
Mrs. RL: Follow up

• After 3 months of treatment, Mrs. RL reported good relief and the medications were tapered off gradually.
WOULD YOU MAKE ANY CHANGES TO THERAPY OR CONDUCT FURTHER INVESTIGATIONS?
Case: Mr. Ali
Mr. Ali: Profile

- 29-year-old male, soldier
- No history of any comorbidities
- Heavy smoker
- Experienced shortness of breath and chest and throat pain during military training
Mr. Ali: Physical Examination

- Heart rate = 110 beats/min
- Blood pressure = 90/45 mmHg
- VAS = 8/10
- Diffuse chest pain
- On and off pain in left arm
- Sweating, pallor
- No GI tract signs or symptoms

GI = gastrointestinal; VAS = visual analog scale
The patient’s pain score is 8
Discussion Questions

Based on the case presentation, what would you consider in your differential diagnosis?
Mr. Ali: Diagnosis

- Inferior wall myocardial infarction
# Somatic vs. Visceral Pain

<table>
<thead>
<tr>
<th>Somatic</th>
<th>Visceral</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Pain originating from skin/skeletal muscle</td>
<td>- Pain originating from organs</td>
</tr>
<tr>
<td>- Evoked by tissue injury</td>
<td>- Not always evoked by tissue injury</td>
</tr>
<tr>
<td>- Can always be stimulated by mechanical injury</td>
<td>- Primarily stimulated by inflammation, distention and ischemia, not mechanical injury</td>
</tr>
<tr>
<td>- Can be superficial (skin, muscle) or deep (joints, tendons, bones)</td>
<td>- Involves hollow organ and smooth muscle nociceptors sensitive to stretching, hypoxia, and inflammation</td>
</tr>
<tr>
<td>- Nociceptors are involved</td>
<td>- Usually referred, dull, poorly localized, vague, and diffuse</td>
</tr>
<tr>
<td>- Sharp, precise; often well localized</td>
<td>- Often referred to somatic regions</td>
</tr>
<tr>
<td>- Usually described as throbbing or aching</td>
<td>- May be associated with autonomic symptoms (e.g., pallor, sweating, nausea, blood pressure and heart rate changes</td>
</tr>
<tr>
<td>- Never referred</td>
<td>-</td>
</tr>
</tbody>
</table>

Visceral Pain
Pain Transmission through Sensory Somatic Afferents

Skin Nociceptors

- $A_\beta$ (large myelinated)
  - $CV= 30-100$ m/s, ~25% of total
- $A_\delta$ (small myelinated)
  - $CV= 6-30$ m/s
- C fiber (small unmyelinated)
  - $CV= 1-2.5$ m/s
- Terminations: Lamina I, IIo, III and V

$CV =$ conduction velocity
Pain Transmission through Sensory Visceral Afferents

Visceral nociceptors

- Aδ (small myelinated)
  - CV = 6-30 m/s
- C fiber (small unmyelinated)
  - CV = 1-2.5 m/s
- Terminations:
  - Lamina I, Ilo, V

CV = conduction velocity
Somatic vs. Visceral Pain

Visceral Pain

• Higher brain centers get “confused” between somatic and visceral origin
  – Myocardial pain (T1-T5) refers to anterior chest wall and down to the medial aspect of the arm (T1-T2)
  – Diaphragmatic and biliary tract pain travels through the PN to terminate at C3-C4
• Pain is referred to dermatomes in the neck and shoulder

NOT all visceral pain is referred

PN = phrenic nerve
Referred Pain: Viscerosomatic Convergence

Viscerosomatic convergence:
Primary afferents from myocardium and somatic region of left arm converge on same projection neuron in spinal cord.

Myocardial Infarction

Brain → Arm Pain

Spinal cord
Discussion Questions

WHAT FURTHER HISTORY WOULD YOU LIKE TO KNOW?

WHAT TESTS OR EXAMINATIONS WOULD YOU CONDUCT?
Mr. Ali: Investigation

- Lab tests: Troponin 1 increased from 0.24 to 1.19 in 24 h (N:0-0.1)
- Normal X-ray
- ECG: sinus rhythm, abnormal T: ischemia
- CT Scan
- Angiography
Mr. Ali: Lab Reports (over 24 h)

<table>
<thead>
<tr>
<th>Clinical Chemistry Report</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Test</strong></td>
</tr>
<tr>
<td>BUN</td>
</tr>
<tr>
<td>Creatinine, serum</td>
</tr>
<tr>
<td>Blood Glucose</td>
</tr>
<tr>
<td>Total Bilirubin</td>
</tr>
<tr>
<td>Alkaline phosphatase</td>
</tr>
<tr>
<td>S.G.P.T. (ALT)</td>
</tr>
<tr>
<td>S.G.O.T. (AST)</td>
</tr>
<tr>
<td>Total Protein</td>
</tr>
<tr>
<td>Albumin</td>
</tr>
<tr>
<td>Globulin</td>
</tr>
<tr>
<td>Calcium</td>
</tr>
<tr>
<td>Sodium</td>
</tr>
<tr>
<td>Potassium</td>
</tr>
<tr>
<td>Chloride</td>
</tr>
<tr>
<td>Total CO2</td>
</tr>
<tr>
<td>CR</td>
</tr>
<tr>
<td>CK</td>
</tr>
<tr>
<td>LDH</td>
</tr>
<tr>
<td>CRP Extended Range</td>
</tr>
<tr>
<td>Troponin I</td>
</tr>
</tbody>
</table>

**Comments:**

TROPOVIN RESULT INFORMED TO ZUBAIDA
Mr. Ali: ECG

Rate: 57
RR: 1053
PR: 174
QRSD: 97
QT: 449
QTcB: 438
QTcF: 441

Rate: 57
RR: 1053
PR: 174
QRSD: 97
QT: 449
QTcB: 438
QTcF: 441

- Sinus rhythm, normal P axis, V-rate 50-99
- Probable left atrial enlargement, P >50ms, <0.10mV V1
- Inferior infarct, old, Q >35ms, II III aVF
- Abnrm T, consider ischemia, anterolateral lds, T <0.20mV, I aVL V2-V6

Unconfirmed Diagnosis

Device: 10016430
Speed: 25 mm/sec
Limb: 10 mm/mV
Chest: 10.0 mm/mV

F 50- 0.50-100 Hz W
PH100B CL P?
Mr. Ali: CT Scan
Mr. Ali: CT Scan
Mr. Ali: CT Scan
Mr. Ali: Angiography
Discussion Question

WHAT TREATMENT STRATEGY WOULD YOU RECOMMEND?
Mr. Ali: Treatment

- Heparin
- Nitroglycerin
- Stenting
Discussion Questions

WHAT OTHER TESTS OR EXAMINATIONS WOULD YOU CONDUCT?
Mr. Ali: Further Testing and Follow-up

- Clinical
- Biological
- Electrical
- Echography
WOULD YOU MAKE ANY CHANGES TO THERAPY OR CONDUCT FURTHER INVESTIGATIONS?


References


